

350 FIFTH AVENUE

NEW YORK 1, N. Y.

1. Budget Plan (first year) 350 FIFTH AVENUE NEW YORK 1, N. Y.  
 2. Personnel: Technician, Animal Care, Salaried  
 3. Materials: Tissue, Glassware, etc. Expandable Subsidies  
 Application For Research Grant  
 Overhead 40%  
 Other

Date: March 8, 1955

1. Name of Investigator: David M. Spain, M.D. - Pathologist  
 Norman Molomut, Ph.D. - Immunologist
2. Titles and Staff Available: Experimental Animal Room; Histological Laboratory; Internal strains of mice; Experimental Histo-Pathology Laboratory; Bacteriology and Bacteriology Laboratory; Microchemistry; Tissue Culture; Microphotography.
3. Institution: Waldemar Medical Research Foundation, Inc.  
 78 Address: 16 Sintsink Drive East  
 Addition to location: Port Washington, N. Y.
4. Project or Subject: Study of Host Factors in Experimental Induction of Pulmonary Tumors in Mice.
5. Additional Requirements:

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):  
 One of the basic problems in the experimental approach to the lung cancer problem is the inability with normal carcinogen to establish adequate base line controls and reproducible results as indicated by the induction of lung cancer. The techniques which have been used to date include the induction of a methylcholanthrene pellet encased in wire mesh with hooks, placed into the bronchial tree through a tracheostomy and the introduction of the methylcholanthrene by means of an impregnated thread drawn through the chest wall into the lung by a fine needle. In the former procedure, it is difficult to eliminate associated infection in the segment of the lung obstructed by the pellet. Furthermore, carcinoma as yet has not been induced with any degree of regularity by this technique. In the latter procedure, since the thread is drawn through the chest wall, subcutaneous carcinoma complicated the picture. It is proposed that we investigate a technique of direct introduction of the carcinogen in a propylene glycol or aerosol solution sprayed with slight pressure with a tracheostomy by means of a fine glass cannula directly into a bronchus. This would eliminate all of the aforementioned complications. Furthermore, with the techniques employed previously, it has been difficult to secure a significant incidence of bronchial carcinoma. It is proposed that enhancing agents such as cortisone, and/or appropriate lyophilized tumor, normal tissue or anti-sera to tumor, be given along with the carcinogen, in order to attempt to establish an adequate incidence of experimental lung cancer. Once this base line control is established, it is then proposed to repeat the procedure with those agents associated with smoking that are considered to be carcinogens. This will be done on various strains of mice and if necessary, various strains of rats.

/s/ Eleanor L. Linder  
 Business Office of the Institution

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5 continued -

If the basic technique here proposed meets with success, since in the process of smoking, areas of the lung are exposed to temporary states of relative anoxia and since individuals in their environment are exposed to carbon monoxide and other fumes which interfere with normal respiratory exchange leading to relative anoxia and since experimentally, Goldblatt and Gey have demonstrated in tissue culture that under conditions of low oxygen tension, normal cells have changed into malignant cells, it is proposed that the above experiments be repeated on animals in closed chambers with controlled oxygen tensions.

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6. Budget Plan: (first year)

Senior Biologist, Technician, Animal Care  
Animals, Feed, Bedding, MCA, glassware, etc.

Salaries

Expendable Supplies

Permanent Equipment

Overhead 10%

Other

\$ 9,250.00

1,500.00

none

1,000.00

300.00

Total, 1955 \$12,050.00

7. Anticipated Duration of Work:

Three years, P.D. - Pathologist

Norman Molomit, Ph.D. - Immunologist

8. Facilities and Staff Available:

Experimental Animal Room; cold room; Biochemical Laboratory; Inbred strains of mice; Lyophilizer; Histo-Pathology Laboratory, Immunology and Bacteriology Laboratory; Spectrophotometry; Tissue Culture; Chromatography.

9. Additional Requirements:

Staff: Pathologist, Oncologist, Immunologist, Biochemist and Pharmacologist in addition to technicians.  
John Washington, N. Y.

10. Additional Information (Including relation of work to other projects and other sources of supply):

Study of Host Factors in Experimental Induction of Pulmonary Tumors in Mice.

11. Additional Requirements:

None

12. Additional Information (Including relation of work to other projects and other sources of supply):

Experimental induction of tumors in animals has been shown through our studies on inflammatory responses including immune phenomena to be definitely related to the status of host function. By means of such agents as cortisone, lyophilized tissue and tumor extracts, and anti-tumor anti-sera, tumors which ordinarily do not grow have been induced to grow and even to metastasize. The enclosed reprints of our own studies and appended bibliographies are pertinent as is the work of Baserga and Shubik (Science 121, 100) and Pomeroy (Cancer Research 14, 201). Recently, Toolan of the Sloan-Kettering Institute, following these same procedures has succeeded in growing human cancers in rats. It is believed that in order to succeed in the experimental induction of lung tumors in animals, that the technique may require some method of intervening in the normal physiologic state of the host. Indeed, this may very well be a clue to the possibility that carcinogenic substances in products such as tobacco smoke, have their influence on hosts in whom other factors of debility are existent.

With a prophylactic by means of a fine glass needle directly into a bronchus would eliminate all of the aforementioned complications. Furthermore, with techniques employed previously, it has been difficult to secure a significant incidence of bronchial carcinoma. It is proposed that enhancing agents such as cortisone, and/or appropriate lyophilized tumor, normal tissue or anti-tumor, be given along with the carcinogen. If adequate incidence of experimental lung tumor is established, it is then proposed to repeat the procedure with agents associated with smoking that are considered to be carcinogenic. This will be done with various strains of mice and if necessary, various stages of work.

Signature: /s/ Norman Molomit

Director of Project

/s/ Florence Lazere  
Business Officer of the Institution

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Reprints Enclosed

1. "Cortisone Effect on Pneumonitis Produced in Mice by Exposure to a High Oxygen Atmosphere", Warshaw, L. J., Molomut, N., and Spain, D. M., Proc. Soc. Exp. Biol. Med., 80, 341 (1952).
2. "Effect of Previously Injected Immune Serum and Tissue on the Survival of Tumor Grafts in Mice", Kaliss, N., Molomut, N., Harriss, J. L. and Gault, S. D., J. Nat. Cancer Inst., 13, 847 (1953).
3. "Induction of Metastases from Sarcoma I in C37 BL/6 Mice", Molomut, N., Spain, D. M., Gault, S. D. and Kreisler, L., Am. J. Pathology, 30, 375-389 (1954).
4. "Preliminary Report on the Experimental Induction of Metastases from a Heterologous Cancer Graft in Mice", Molomut, N., Spain, D. M., Gault, S. D. and Kreisler, L., Proc. Nat. Acad. Sciences, 38, 991 (1952).
- 5 "Some Basic Biologic Effects of Cortisone as Related to Pulmonary Disease" Spain, David M., Diseases of the Chest, 23, 270 (1953).

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